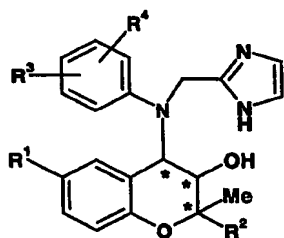


WHAT IS CLAIMED IS :

1. Benzopyran derivatives substituted with secondary amines including imidazole by the following formula 1, their stereochemical isomers and their pharmaceutically acceptable salts.

FORMULA 1



Wherein

R<sup>1</sup> represents H, CN, NO<sub>2</sub> or NH<sub>2</sub>,

10 R<sup>2</sup> represents CH<sub>3</sub>,  $\begin{array}{c} \text{OR}^a \\ | \\ \text{CH} \\ | \\ \text{OR}^a \end{array}$ , or  $\begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{CH} \quad \text{Z} \\ \diagdown \quad \diagup \\ \text{O} \end{array}$ ; R<sup>a</sup> represents straight or branched alkyl group of C<sub>1</sub>-C<sub>4</sub>; and Z is straight or branched alkyl group of C<sub>2</sub>-C<sub>6</sub>,

R<sub>3</sub> and R<sub>4</sub> are independent each other and represent H, Cl, Br, F, alkyl group of C<sub>1</sub>-C<sub>3</sub>, OR<sup>b</sup>, CF<sub>3</sub>, OCF<sub>3</sub>, NO<sub>2</sub>, or  
15 CO<sub>2</sub>R<sup>b</sup>; R<sup>b</sup> represents H or alkyl group of C<sub>1</sub>-C<sub>3</sub>,  
and \* represents the chiral center.

2. Benzopyran derivatives substituted with secondary amines including imidazole, their stereochemical isomers and their  
20 pharmaceutically acceptable salts according to claim 1,

wherein the compound of formula 1 is selected from the group consisting of:

- 1) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[N-(4-chlorophenyl)-N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 2) (2S,3R,4S)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[N-(4-chlorophenyl)-N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 3) (2R,3R,4S)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[N-(4-chlorophenyl)-N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 4) (2R,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[N-(4-chlorophenyl)-N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 5) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[N-(4-trifluoromethylphenyl)-N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 6) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[N-(4-methoxyphenyl)-N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 7) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[N-(4-trifluoromethoxyphenyl)-N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 8) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-

2-methyl-6-nitro-4-[N-(4-bromophenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

9) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-

2-methyl-6-nitro-4-[N-(2,4-dimethylphenyl)-

5 N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

10) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-

hydroxy-2-methyl-6-nitro-4-[N-(2-isopropylphenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

11) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-

10 hydroxy-2-methyl-6-nitro-4-[N-(2,3-dimethylphenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

12) (2R,3R,4S)-3,4-dihydro-2-dimethoxymethyl-3-

hydroxy-2-methyl-6-nitro-4-[N-(2,3-dimethylphenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

15 13) (2R,3R,4S)-3,4-dihydro-2-dimethoxymethyl-3-

hydroxy-2-methyl-6-nitro-4-[N-(4-bromophenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

14) (2R,3R,4S)-3,4-dihydro-2-dimethoxymethyl-3-

hydroxy-2-methyl-6-nitro-4-[N-(4-methoxyphenyl)-

20 N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

15) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-

hydroxy-2-methyl-6-nitro-4-[N-(4-fluorophenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

16) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-

- hydroxy-2-methyl-6-nitro-4-[*N*-(2-methoxyphenyl)-  
*N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 17) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-  
hydroxy-2-methyl-6-nitro-4-[*N*-(2-isopropylphenyl)-  
5 *N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 18) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-  
hydroxy-2-methyl-6-nitro-4-[*N*-(2-methoxyphenyl)-  
*N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 19) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-  
10 hydroxy-2-methyl-6-nitro-4-[*N*-(3-chlorophenyl)-  
*N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 20) (2*S*, 3*S*, 4*R*)-3,4-dihydro-2-dimethoxymethyl-3-  
hydroxy-2-methyl-6-nitro-4-[*N*-(3-chlorophenyl)-  
*N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 21) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-  
15 hydroxy-2-methyl-6-nitro-4-[*N*-(4-trifluoromethoxyphenyl)-  
*N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 22) (2*S*, 3*S*, 4*R*)-6-cyano-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[*N*-(4-chlorophenyl)-  
20 *N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 23) (2*R*, 3*R*, 4*S*)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[*N*-(4-chlorophenyl)-  
*N*-(1*H*-imidazol-2-ylmethyl)amino]-2*H*-1-benzopyran;
- 24) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-

- 3-hydroxy-2-methyl-4-[N-(4-chlorophenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 25) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[N-(4-trifluoromethylphenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 5 26) (2R,3R,4S)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[N-(4-trifluoromethoxyphenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 27) (2R,3R,4S)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
10 3-hydroxy-2-methyl-4-[N-(2,3-dimethylphenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 28) (2R,3R,4S)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[N-(4-methoxyphenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 15 29) (2R,3R,4S)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[N-(4-bromophenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 30) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[N-(2,3-dimethylphenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 20 31) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-  
3-hydroxy-2-methyl-4-[N-(2-methoxyphenyl)-  
N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;
- 32) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-

3-hydroxy-2-methyl-4-[N-(4-methoxyphenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

33) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-

3-hydroxy-2-methyl-4-[N-(2,4-dimethylphenyl)-

5 N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

34) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-

3-hydroxy-2-methyl-4-[N-(2-isopropylphenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

35) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-

10 3-hydroxy-2-methyl-4-[N-(4-trifluoromethoxyphenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran;

36) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-

3-hydroxy-2-methyl-4-[N-(4-bromophenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran; and

15 37) (2S,3S,4R)-6-amino-3,4-dihydro-2-dimethoxymethyl-

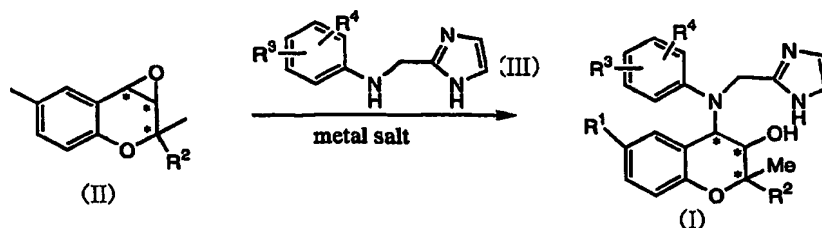
3-hydroxy-2-methyl-4-[N-(4-fluorophenyl)-

N-(1H-imidazol-2-ylmethyl)amino]-2H-1-benzopyran.

3. A process for preparing the benzopyran derivatives  
20 substituted with secondary amines including imidazole of  
claim 1, comprising the step of reacting an epoxide  
compound (II) with a secondary amine compound including  
imidazole (III) in the presence of a metal salt in an  
reaction solvent to obtain a compound (I), as described in

scheme 1.

Scheme 1



Wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  \* and  $n$  are each defined as  
5 above claim 1.

4. The process according to claim 3, wherein the metal salt  
is selected from the group consisting of  $Mg(ClO_4)_2$ ,  $CoCl_2$ ,  
 $LiClO_4$ ,  $NaClO_4$ ,  $CaCl_2$ ,  $ZnCl_2$ ,  $LiBF_4$ , and  $Zn(Tf)_2$ .

10

5. The process according to claim 3, wherein the reaction  
solvent is selected from the group consisting of  
acetonitrile, tetrahydrofuran, and dimethylformamide.

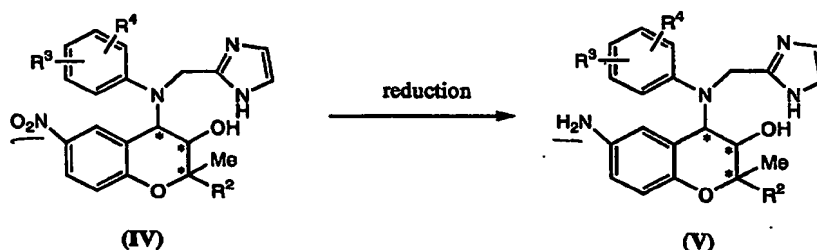
15 6. A process for for preparing the benzopyran derivatives  
substituted with secondary amines including imidazole of  
claim 1, comprising the step of

1) reduction of the nitro compounds (IV) by  
hydrogenation using metal catalysts such as platinum,  
20 palladium, palladium on carbon (Pd/C), Raney-nickel, etc.  
in a suitable solvent, to obtain the amino compound (V) as

described in scheme 4, below; or

- 2) reduction of the nitro compounds (IV) using an reducing agent in the presence of  $\text{CuSO}_4$ ,  $\text{Cu}(\text{OAc})_2$ ,  $\text{CoCl}_2$ ,  $\text{SnCl}_2$  or  $\text{NiCl}_2$ , to obtain the amino compound (V) as
- 5 described in scheme 4, below.

Scheme 4



Wherein  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$  and \* are each defined as above

10 claim 1.

7. The process according to claim 6, wherein the reducing agent is  $\text{NaBH}_4$ .

15 8. Pharmaceutical compositions pharmacologically useful for treatment of cancer, diabetic retinopathy, and rheumatoid arthritis by suppressing angiogenesis, which contain the benzopyran derivatives substituted with secondary amines including imidazole of claim 1 or their pharmaceutical

20 acceptable salts as an active ingredient.

9. Pharmaceutical compositions pharmacologically useful as



neuroprotectives for prevention and treatment of infant asphyxia, glaucoma, diabetic neuropathy, and head trauma, which contain the benzopyran derivatives substituted with secondary amines including imidazole of claim 1 or their  
5 pharmaceutical acceptable salts as an active ingredient.

10. Pharmaceutical compositions pharmacologically useful as anti-oxidants for prevention and treatment of neurodegenerative diseases including aging, senile dementia,  
10 and atherosclerosis, which contain the benzopyran derivatives substituted with secondary amines including imidazole of claim 1 or their pharmaceutical acceptable salts as an active ingredient.

15 11. Pharmaceutical compositions pharmacologically useful as cardioprotectives for prevention and treatment of myocardiac infarction, heart failure, and angina pectoris, which contain the benzopyran derivatives substituted with secondary amines including imidazole of claim 1 or their  
20 pharmaceutical acceptable salts as an active ingredient.